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Applicant's Name: James T. English, et al.

Serial No.: 09/829,549 **Examiner:** T. Wessendorf

Filing Date: 04/10/01 **Art Unit:** 1639 **Confirmation No.:** 8198

Application Title: PHAGE DISPLAY SELECTION OF ANTI FUNGAL PEPTIDES

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FEE TRANSMITTAL

Application Number 09/829,549 Art Unit 1639
Filing Date April 10, 2001 Confirmation No. 8198
Inventor(s) James T. English, et al.
Examiner Name Teresa D. Wessendorf
Attorney Docket Number UMO 1521.1

☒ Applicant claims small entity status.

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☒ Notice of Appeal
☐ Filing a brief in support of appeal
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UMO 1521.1
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: James T. English, et al. Art Unit: 1639
Serial No.: 09/829,549
Filed: April 10, 2001
Confirmation No.: 8198
For: PHAGE DISPLAY SELECTION OF ANTI FUNGAL PEPTIDES
Examiner: Teresa D. Wessendorf

December 22, 2005

PRE-APPEAL BRIEF REQUEST FOR REVIEW

TO THE COMMISSIONER FOR PATENTS:
SIR OR MADAM:

Applicants hereby request review of the Office's rejection of claims 1-9 and 32-51 as set forth in the final Office action dated July 25, 2005. A Notice of Appeal is being filed concurrently herewith.

While no fees are believed due with respect to this Request, the Commissioner is authorized to charge any fees due to Deposit Account No. 19-1345.

ARGUMENTS

For each of the claims discussed below, the Examiner's rejection is clearly erroneous and fails to establish a *prima facie* case of obviousness. Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion, or incentive supporting the combination. If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.[1]

Claim 1 Obviousness Rejection

Claim 1 is directed to a method for identifying non-immunoglobulin peptides having an affinity for the surface of a fungus. Among other things, the method comprises constructing a library of peptides by inserting random oligonucleotides into a vector, and transfecting a host cell

[1] MPEP § 2143.01.

with the vector to amplify the vector in an infectious form, creating a library of peptides on the surface of the vector. The vector is contacted with a target fungus, and the vector that binds to the fungus is eluted and amplified. The oligonucleotides contained in the eluted vector are sequenced, and the amino acid sequence of peptides encoded by the oligonucleotides is deduced. The non-immunoglobulin peptides for which the amino acid sequence has been deduced are then selected.

Gough et al.

Gough et al. describe methods for the identification of antibodies specific for surface-exposed epitopes on germlings of certain species of *Phytophthora* to be used for production of immunological probes and scFV antibodies which interfere with the infection process.[2] Gough et al. do not disclose the display of a random peptide library on a vector (e.g., phage), or the selection of non-immunoglobulin peptides that bind epitopes on the surface of a fungus, as required by claim 1.

Gough et al. use only scFV antibody fragments in their disclosed phage display methods, and report no problems with the use of antibody fragments for their objectives (i.e., identifying antibodies that have surface specificity to *Phytophthora* species).[3] Not only does Gough et al. fail to suggest the use of peptides in the disclosed methods, the substitution of peptides for antibody fragments would be unproductive as Gough et al. seek to identify antibodies, not mere peptides.[4]

The Office notes that Gough et al. refer to similar strategies that have been applied to the selection of phage-displayed peptides that bind to the surface receptors of intact platelets.[5] This reference, however, implies that mere peptides would be inadequate to accomplish the clearly-stated objectives of Gough et al. To isolate antibodies to surface antigens for use as immunological probes per Gough et al., one skilled in the art could not, and would not modify the disclosed methods so as to substitute random, non-immunological peptides for antibody fragments.

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[2] Gough et al. at page 98.
[3] Id.
[4] See further arguments in May 6, 2005, Amendment E, pages 8-9; see also Gough et al. at page 107.
[5] July 25, 2005, Office action, page 4; see also Gough et al. at page 98.

Kodadek

Kodadek describes methods of isolating small peptides that recognize specific target peptides for use in affinity purification. Put simply, Kodadek and Gough et al. cannot be combined without violating the objectives of either reference.[6] Incredibly, the Office asserts that Kodadek, by recognizing the disadvantages in the use of antibodies, provided the motivation to one skilled in the art to substitute simple peptides into the methods of Gough et al.[7] Kodadek, however, directly contradicts the Office's position: early efforts by Kodadek and his co-workers to isolate small peptides using well-established phage display methods "failed completely."[8]

After encountering first-hand the limitations and/or failure of antibodies and phage display, Kodadek resorted to an elaborate genetic selection scheme to identify certain library encoded peptides having affinity to a target peptide. In brief, Kodadek's genetic selection scheme involves forming two compatible constructs, one encoding the target peptide, and the other encoding a library of DNA fragments, and transforming them into *E. coli*.[9] If a library encoded peptide (hereinafter "LEP") is present in the library that associates with the target peptide, a complex between the LEP and the target is formed.[10] The complex blocks certain operator regions in *E. coli*, making it resistant to a bacterial infection challenge.[11] Resistant colonies may then be selected, and the LEPs that bind to the target isolated.[12]

Kodadek further describes that, in some cases, even the genetically selected LEPs may not possess the desired level of affinity for the target.[13] In this event, Kodadek describes that conventional phage display methods may be modified by attaching the genetically selected LEP to the end of a standard phage displayed peptide library to form a "pincer."[14] The affinity of the genetically selected LEP is improved by the addition of the phage displayed peptide because the LEP arm and the phage displayed random peptide library arm wrap around the target peptide.[15] Kodadek's specialized "pincer" approach thus facilitates identification of peptide-target

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[6] See further arguments in May 6, 2005, Amendment E, pages 9-10.
[7] See, e.g., February 9, 2005, Office Action, pages 3-4.
[8] Kodadek, page 4, paragraph [0038].
[9] Id. at paragraph [0042].
[10] Id.; see also Fig. 1.
[11] Id.
[12] Id.
[13] See Kodadek, pages 13-14, paragraph [0125]-[0134].
[14] See Kodadek, page 14, paragraph [0132].
[15] Id. at paragraphs [0132]-[0133]; see also Fig. 7.

interactions where the original peptide-epitope interaction (i.e., the LEP-target interaction in the genetic selection scheme) is insufficient for stable association.[16]

Upon a careful reading of Kodadek, summarized above, one of skill in the art would not, and could not be motivated to substitute the use of random, non-immunological peptides for scFV antibody fragments in the method of Gough et al. First, Kodadek refers to the futile attempts to identify peptide complexes using phage display that, in his words, "failed completely." Kodadek then describes an elaborate genetic selection scheme designed to be an improved method, in and of itself, to overcome past failures in identifying peptide complexes (e.g., using phage display). It is only after particular LEPs are identified by the genetic selection scheme (i.e., on the basis of affinity) that Kodadek couples them with conventional phage display methods to form a pincer. In claim 1, conversely, peptides of unknown affinity alone are expressed in the phage. Thus Kodadek clearly implies that conventional phage display methods, standing on their own, would not work. Why else would Kodadek go to all the trouble of devising the genetic selection scheme if random peptide phage display alone would be effective?

Petrenko et al.

Petrenko et al. describe methods of forming phage displayed "landscape libraries" having complex surface functions. According to Petrenko et al., the complex surface functions of phage clones depend on interactions between neighboring groups of display peptides and wild type peptides.[17] The emergent properties of the phage surface inhere (i.e., are intrinsic) in the entire surface of the phage, not in the peptides themselves.[18] Stated another way, Petrenko et al. are describing modifications to phage such that the phage will display "global properties" across the entire surface of the phage, not only mere localized properties at the particular displayed peptides. Two specific examples of such global properties are described in Petrenko et al., chloroform resistance and metal ion affinity.[19]

One skilled in the art would not be motivated to modify the methods of Gough et al. according to the methods described in Petrenko et al., as such a modification would fail to achieve the clearly-stated objectives of each reference. As described above and elsewhere, Gough et al. are seeking to identify specific antibodies that bind to the surface of *Phytophthora*.

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[16] Id.
[17] Petrenko et al. at page 797.
[18] Id.
[19] Id. at pages 798-799, 801; see also May 5, 2005, Amendment E, page 11.

In contrast, Petrenko et al. are attempting to identify phage clones that exhibit global properties across the entire phage surface (e.g., chloroform resistance), irrespective of the particular peptides of the phage displayed library. At no point in Petrenko et al. is there any discussion or disclosure about how the localized properties of phage-peptide interactions provide an advantage over phage-antibody fragments; it is not enough that peptide libraries could be theoretically substituted into the methods of Gough et al.[20]

Because the subject matter of the base claim is nonobvious, the subject matter of claims 2-9 and 32-47 would thus also be nonobvious. To the extent claims 48 and 49 include the same features as claim 1, they are nonobvious for the same reasons as claim 1. Because they depend from a nonobvious base claim, claims 50 and 51 would thus also be nonobvious.

CONCLUSION

For at least these reasons, Applicants respectfully request allowance of all pending claims.

Respectfully submitted,

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[20] See MPEP § 2143.01 (The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art suggests the desirability of the combination.").